



EDWARD M. JOHNSON
THE MOUNT SINAI MEDICAL CENTER

ONE GUSTAVE L. LEVY PLACE • NEW YORK, N.Y. 10029



Mount Sinai School of Medicine • The Mount Sinai Hospital

Brookdale Center for Molecular Biology

5-25-88

Dear Dr. Leiberman,

Thank you for your recent note and the reference on the tungsten microprojectiles. Also, thank you again for agreeing to submit our article (Appel et al.; "Asbestos, ^{Fibers} Mediates...") to PNAS. I want to answer a few of your queries.

We have thought of patenting an asbestos transfection process, but when we brought it up with a couple of companies, none seemed very interested. Also, one potential problem might be that we published an abstract on this at the FASEB meeting more than a year ago.

There are a scattering of other papers in the literature regarding use of abrasives or minerals to assist in transfection. You recall the Fraenkel-Conrat papers using carbonundum on tobacco leaves. There was also a paper by Singer and Fraenkel-Conrat using Bentonite (*Virology* 14, 59-65; 1961). I think Bentonite is high in aluminum silicate. George Dubes

(2)

published a paper, referred to in our article, on the use of various mineral silicates to enhance uptake of viral RNA into cells. I believe Dubes was actually the first to transfect using calcium phosphate, as well.

There are several ways to explain the synergism with smoking, but nothing very easily testable. The explanation we favor is that different oncogenes (or sets of oncogenes) might be activated by either asbestos or smoking. Each separately must await some additional event(s) to be oncogenic, but together they are sufficient or more nearly so. The precedent ~~would be~~^{is} cooperation between myc and ras oncogenes. Of course this is total speculation, but not outrageous. One might expect that mutation by chemical carcinogens through smoking would affect different DNA sequences than mutation by DNA integration following transfection.

Tom Fary (who is a pathologist here and the actual asbestos expert - my work being primarily on DNA replication; Tom was also at Rockefeller) intends to follow up this work with animal asbestos inhalation experiments using myc and ras oncogenes found to chrysotile. That would directly demonstrate that transfection with asbestos could cause cancer. As an alternative to inhalation, he is also thinking of intraperitoneal injection since

(3)

that could affect the mesothelium.

We have now received the comments of reviewer #1 (thank you for conveying them), and we eagerly await those of the second reviewer. I realize that you are busy, and we are sincerely grateful for the time you have devoted.

Sincerely,
Edwin Jor